



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,371	07/26/2006	Ho Sung Cho	AMBX-0028.00US	1687

45811 7590 03/06/2009  
ATTN: JOHN W. WALLEN, III  
AMBRX, INC.  
10975 NORTH TORREY PINES ROAD  
SUITE 100  
LA JOLLA, CA 92037

EXAMINER
----------

SHAFFER, SHULAMITH H

ART UNIT	PAPER NUMBER
----------	--------------

1647

MAIL DATE	DELIVERY MODE
-----------	---------------

03/06/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/587,371	<b>Applicant(s)</b> CHO ET AL.	
	<b>Examiner</b> SHULAMITH H. SHAFER	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-83 is/are pending in the application.
- 4a) Of the above claim(s) 1-43, 46-58 and 62-83 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 44, 45 and 59-61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/7/08, 2/1/08, 10/9/08</u> .                                 | 6) <input type="checkbox"/> Other: _____                          |

## **Detailed Action**

### ***Status of Application, Amendments, And/Or Claims:***

#### ***Restriction Requirement:***

Applicants' election of Group II, claims 44, 45, and 59-61, drawn to an isolated nucleic acid comprising a polynucleotide that encodes a 4HB polypeptide, a host cell comprising said nucleic acid and a method of making a 4HB polypeptide recombinantly, in response of 16 December 2008 is acknowledged. In response to requirement for species election, applicants elect the amber, ochre and opal codons as selector codons. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-83 are pending in the instant application. Claims 1-43, 46-58 and 62-83 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 44, 45, and 59-61 are under consideration to the extent they read on the elected invention.

#### ***Information Disclosure Statement:***

The Information Disclosure statements (IDS) submitted on the 7 January 2008, 1 February 2008 and 9 October 2008 have been considered. The signed copies are attached.

## **Objections**

#### ***Specification:***

The specification is objected to as having two duplicate pages identified as page 205.

Art Unit: 1647

***Claims:***

Claims 44 and 61 are objected to as reciting the acronym "4HB polypeptide". The claims should recite the full name of the polypeptide the first time it is used. It is suggested that the claims be amended to read, for example, "a four helical bundle (4HB) polypeptide".

**Rejections**

***35 U.S.C. § 101:***

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 59 and 60 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 59 and 60, as recited, read on host cells, including any eukaryotic cell. There is no limitation wherein the host cells are isolated or in culture; therefore the claims read on transfected cells in a human, and thus are not patentable subject matter. This rejection could be overcome by adding a limitation wherein the host cells are isolated or in culture.

***35 U.S.C. § 112, Second Paragraph:***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 61 is vague and indefinite in reciting "non-naturally encoded amino acids". The specification teaches the term "non-naturally encoded amino acid" refers to an amino acid that is not one of the 20 common amino acids or pyrrolysine or selenocysteine. The term "non-naturally encoded amino acid" also includes, but is not limited to, amino acids that occur by modification (e.g. post-translational modifications) of a naturally encoded amino acid (including but not limited to, the 20 common amino acids or pyrrolysine and selenocysteine) [paragraph 0158 of PGPUB 20080300163, the PGPUB of the instant invention]. This is not a limiting definition; one of ordinary skill in the art could not determine which amino acids are included in the definition. Thus, the metes and bounds of the claims cannot be determined.

The remainder of the claims is included in this rejection as dependent upon rejected claims.

### ***35 U.S.C. § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### ***Written Description***

Claims 44, 45, 59-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph.

The claims are broadly drawn to an isolated nucleic acid comprising a polynucleotide that encodes a 4HB polypeptide wherein the polynucleotide comprises at

least one selector codon, a cell comprising said nucleic acid and a method of recombinantly making a 4HB polypeptide comprising a non-naturally encoded amino acid.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claims indicates that these claims are drawn to a genus and a method of using said genus, the genus being an isolated polynucleotide that encodes a 4HB polypeptide, wherein the polynucleotide comprises at least one selector codon.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus.

There are four species, polynucleotides encoding human growth hormone, interferon, erythropoietin and G-CSF comprising a non-naturally encoded amino acid disclosed that is within the scope of the claimed genus (Table 8) *i.e* an isolated polynucleotide that encodes a 4HB polypeptide, wherein the polynucleotide comprises at least one selector codon; these polypeptides are disclosed in great detail in the specification, and back translation from polypeptide sequences to nucleic acid sequences is well-known in the art. The disclosure of several species may provide an

Art Unit: 1647

adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompass numerous species that are not further described as there are many polynucleotides encoding proteins comprising the Growth Hormone Supergene family which comprise polypeptides comprising a four helical bundle [paragraph 0003]. The claims and the disclosure also encompass polynucleotides encoding members of the family yet to be described [paragraph 0003].

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is an isolated polynucleotide that encodes a 4HB polypeptide, wherein the polynucleotide comprises at least one selector codon.

The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of constructing the polynucleotide. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polynucleotides comprising selector codons, that encode a 4HB polypeptide wherein the 4HB polypeptide is human growth hormone, interferon, erythropoietin and G-CSF but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

### ***Enablement***

Claims 44, 45 and 59-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising a polynucleotide (wherein the polynucleotide comprises at least one selector codon) that encodes a 4HB polypeptide wherein the polypeptide is Growth hormone, interferon, G-CSF and erythropoietin as listed on Table 8 of the specification, does not reasonably provide enablement for an isolated nucleic acid of comprising a polynucleotide that encodes any 4HB polypeptide comprising a selector codon at any, unspecified position. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to an isolated nucleic acid comprising a 4HB polypeptide wherein the polynucleotide comprises at least one selector codon. The language of the claims encompasses a nucleic acid which encodes any 4HB polypeptide wherein the selector codon is at any, unspecified position.

The specification teaches the growth hormone (GH) supergene family represents a set of proteins with similar structural characteristics. Each member of this family of proteins comprises a four helical bundle and are thus referred to as "four helical bundle polypeptides" or "4HB" polypeptides. While there are still more members of the family yet to be identified, some members of the family include the following: growth hormone, prolactin, placental lactogen, erythropoietin (EPO), thrombopoietin (TPO), interleukin-2 (IL-2), IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-10, IL-11, IL-12 (p35



Art Unit: 1647

subunit), IL-13, IL-15, oncostatin M, ciliary neurotrophic factor, leukemia inhibitory factor, alpha interferon, beta interferon, gamma interferon, omega interferon, tau interferon, epsilon interferon, granulocyte-colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), macrophage colony stimulating factor (M-CSF) and cardiotrophin-1 (CT-1). Members of the GH supergene family have similar secondary and tertiary structures, despite the fact that they generally have limited amino acid or DNA sequence identity [paragraph 0003 of PG PUB 20080300163, the PG PUB of the instant invention. Thus, the teachings encompass not only a myriad of known polypeptides to be encoded by the polynucleotides of the instant invention, but also polypeptides yet to be identified. Details are presented as to the structure of the following polypeptides: human growth hormone, interferon alpha, granulocyte colony stimulating factor (G-CSF) and erythropoietin, modifications which may be made in the amino acid chains, and encoding polynucleotides [paragraphs 0004-0028]. The specification teaches incorporation of non-naturally encoded amino acids at a number of specific positions in the above enumerated polypeptides [paragraphs 0045-0058]. The disclosure also teaches isolated nucleic acids comprising a polynucleotide that hybridizes under stringent conditions to SEQ ID NO: 21, 22, 26, 27, 31, 32, 33, 34, 40, 41, 42, or 43 wherein the polynucleotide comprises at least one selector codon [paragraph 0066], which are all nucleic acids encoding human growth hormone, interferon alpha, granulocyte colony stimulating factor (G-CSF) and erythropoietin. The 4HB polypeptides comprising a sequence shown in SEQ ID NO: 1, 2, 3, or any other GH polypeptide sequence, SEQ ID NO: 23, 24, 25 or any other hIFN polypeptide sequence, SEQ ID NO: 28, 29, 30, 35, 36, or any other hG-CSF polypeptide sequence, SEQ ID NO: 37, 38, 39, or any other hEPO polypeptide sequence, except that at least one amino acid is substituted by a non-naturally encoded amino acid is also taught. In some embodiments, the non-naturally encoded amino acid is substituted at a position selected from the group consisting of residues 1-5, 82-90, 117-134, and 169-176 from SEQ ID NO: 3 (hGH), or at a position selected from the group consisting of residues 1-16, 30-109, 125-175 as in SEQ ID NO: 29 (G-CSF), or the corresponding amino acid position of SEQ ID NO: 28, 30, 35, or 36, or substitution

Art Unit: 1647

at a position 1-6, 21-40, 68-89, 116-136, 162-166 from SEQ ID NO: 38 (EPO), or SEQ ID NO: 39, or the corresponding amino acid position of SEQ ID NO: 37 [paragraph 0080].. However, insufficient guidance is presented to allow one of ordinary skill in the art to make and use the myriad of other polynucleotides encoding 4HB polypeptides comprising at least one non-naturally encoded amino acid and to test all possible variants without undertaking undue experimentation.

The claims encompass variant nucleic acids that encode variant polypeptides. These claims are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the required biological characteristics of a 4HB polypeptide, since the claims encompass nucleic acids encoding both known and undiscovered members of the growth hormone (GH) supergene family. While the claims are directed to variant nucleic acids encoding polypeptides, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible encoded variants of the unnamed polypeptides. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mickle et al. (2000, Med Clin North Am 84:597-607) teach that cystic fibrosis (CF) is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (page 597). In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving rise to the CF phenotype, thus showing that even the substitution of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, Yan et al. (2000, Science 290:523-527) teach that in certain cases, a change of only two amino acid residues in a protein results in switching the binding of the protein from one receptor to another. Thus, substitution of a selector codon and incorporation of at least one non-naturally encoded amino acid at any unspecified position in any, unidentified polypeptide would have unpredictable effects. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely

Art Unit: 1647

complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded protein are lacking, it is unpredictable as to which variations would result in a functioning polypeptide. Applicants are required to enable one of skill in the art to make and use the claimed invention. It would require undue experimentation for one of skill in the art to make and use the claimed nucleic acids. Since the claims do not enable one of skill in the art to make and use the claimed nucleic acids, but only teaches how to screen for the claimed nucleic acids, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, would result in a functioning polypeptide.

Due to the large quantity of experimentation necessary to determine which of polynucleotides (comprising a selector codon) encoding any 4HB polypeptide comprising a non-naturally encoded amino acid would encode a functional polypeptide, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing that substitutions of even a single amino acid may have drastic effects on the functioning of the polypeptide and the breadth of the claims which fail to recite specific polynucleotides encoding specific polypeptides comprising at least one non-naturally encoded amino acid at identified positions, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

**35 U.S.C. § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1647

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44, 45, and 59-61 are rejected under 35 U.S.C. 102(e) as being anticipated Schultz et al. (US 2003/0082575, filed 10 April 2002, the '575 reference, cited on IDS of 29 October 2008, reference 1 of US PAT Applications).

The '575 reference teaches an isolated nucleic acid comprising at least one selector codon, wherein the selector codon may be the amber codon. The isolated nucleic acid encodes a therapeutic protein which may be an interferon, erythropoietin (EPO), G-CSF or human growth hormone, thus anticipating the limitations of claims 44 and 45. The reference teaches method of making the 4HB polypeptide recombinantly, utilizing a translation system comprising an orthogonal tRNA (O-tRNA) and an orthogonal tRNA synthetase (O-RS), thus anticipating the limitations of claims 59-61. The '575 reference teaches method for making and using translation systems that can incorporate unnatural amino acids into protein [paragraph 0024]. The translation system comprises an orthogonal tRNA (O-tRNA) and an orthogonal tRNA synthetase (O-RS), as required by claim 69. The translation system inserts the unnatural amino acid into a protein produced in the system, in response to an encoded selector codon [paragraph 0025]. The translation systems include cells, such as bacterial cells (e.g., Escherichia coli), archaeobacterial cells, eukaryotic cells (e.g., yeast cells, mammalian cells, plant cells, insect cells) [paragraph 0026], as recited in claim 59. The reference teaches selector codons to insert unnatural amino acids; the selector codon may be an amber codon [paragraph 0031], as required by claim 45. The reference teaches methods for producing at least one protein in a translation system such that the protein comprises at least one unnatural amino acid. In the methods, the translation system is provided with at least one nucleic acid comprising at least one selector codon, wherein the nucleic acid encodes the at least one protein. The translation system is also provided with an orthogonal tRNA (O-tRNA), that functions in the translation system and

Art Unit: 1647

recognizes the at least one selector codon and an orthogonal tRNA synthetase (O-RS) [paragraph 0036]. The methods described may be used to generate large quantities of purified mutant proteins [paragraph 0097]. Among the proteins to be synthesized by the disclosed method are proteins that are homologous to a therapeutic protein; the therapeutic proteins may be an interferon, erythropoietin (EPO), G-CSF and human growth hormone [paragraph 0033]; these proteins are identified in the specification as 4HB polypeptides.

Therefore, the teachings of the '575 reference anticipate all the limitations of claims 44, 45, and 59-61.

Claims 44, 45, and 59-61 are rejected under 35 U.S.C. 102(e) as being anticipated Chin et al. (US 2005/0009049, filed 16 April 2004, priority claimed to provisional applications 60/463,869 (filed 4/17/03), 60/479,931 (filed 6/18/03), 60/493,014 (filed 8/5/03) and 60/496,548 (filed 8/5/03), the '049 reference).

The '049 reference teaches a nucleic acid that comprises a polynucleotide that encodes a polypeptide of interest [paragraph 0016] which may be an interferon, erythropoietin (EPO), human growth hormone, and a G-CSF, which are all polypeptides disclosed as 4HB polypeptides by the specification of the instant invention [paragraph 0038]. The polynucleotide comprises a selector codon that is recognized by the O-tRNA. The selector codon may be a stop codon (e.g., an amber codon, an ochre codon, or an opal stop codon) [paragraph 0047]. Thus the limitations of claims 44 and 45 are anticipated.

The '049 reference teaches compositions of orthogonal tRNAs, orthogonal synthetases and pairs thereof, in eukaryotic cells and methods of producing proteins in eukaryotic cells that include unnatural amino acids [paragraph 0003]. The eukaryotic cell comprises an orthogonal tRNA synthetase (O-RS), an orthogonal tRNA (O-tRNA), and a nucleic acid that comprises a polynucleotide that encodes a polypeptide of interest [paragraph 0016]. The '049 reference teaches methods for producing, in a eukaryotic cell, at least one protein comprising at least one unnatural amino acid. The

Art Unit: 1647

methods include, growing, in an appropriate medium, a eukaryotic cell that comprises a nucleic acid that comprises at least one selector codon and encodes the protein of interest. The eukaryotic cell also comprises an orthogonal tRNA (O-tRNA) that functions in the cell and recognizes the selector codon and an orthogonal tRNA synthetase (O-RS) [paragraph 0042]. The reference also teaches purification of the recombinant proteins produced by the referenced methods [paragraph 0219]. Therefore, the limitations of claims 59-61 are anticipated.

Thus, the teachings of the '049 reference anticipates all the limitations of claims 44, 45, and 59-61.

***Conclusion:***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHULAMITH H. SHAFER whose telephone number is (571)272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1647

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. H. S./  
Examiner, Art Unit 1647

/Manjunath N. Rao, /  
Supervisory Patent Examiner, Art Unit 1647